

REMARKS/ARGUMENTS

Reconsideration of the subject application is respectfully requested.

Claims 1-15 were pending as of the Office Action mailing date of June 12, 2008.

Applicant amends herein independent claim 13 and has cancelled claims 16, 17, 22, and 23. No new matter has been added by any of the amendments.

In view of MPEP 707.07 that requires the Action to be complete as to all matters, Applicant proceeds under the understanding that the present claims are patentable once the references cited herein are overcome.

I. REJECTION UNDER 35 USC 112, 2nd paragraph

Claims 13-32 have been rejected under 35 USC 112, 2nd paragraph. Applicant respectfully traverses this rejection based on currently amended claim 13.

The current invention, as now claimed, is a process that requires:

...combined for recrystallizing and the stereoisomer to be isolated in each case is precipitated and obtained in enriched form a solvent is selected from the group consisting of branched and unbranched alcohols having one to four carbon atoms, acetone, butanone and acetonitrile in each case in the precipitate being used, and/or those tertiary, basic diastereomer mixtures are employed in the quaternization which lead to the abovementioned quaternary diastereomer mixtures, and the stereoisomer to be isolated in each case is obtained in enriched form as a precipitate after the reaction, a first solvent selected from methanol and/or ethanol in which the diastereomer mixture dissolves readily is used for the recrystallization and a second solvent selected from ethyl

acetate and/or tert-butyl methyl ether causing crystallization being used. (amended claim 13)

Claim 13 has been amended to the require substrates combined for recrystallizing and the stereoisomer to be isolated in each case is precipitated and obtained in enriched form, a solvent is selected from the group consisting of branched and unbranched alcohols having one to four carbon atoms, acetone, butanone and acetonitrile in each case in the precipitate being used; and the stereoisomer to be isolated in each case is obtained in enriched form as a precipitate after the reaction, a first solvent selected from methanol and/or ethanol in which the diastereomer mixture dissolves readily is used for the re-crystallization and a second solvent selected from ethyl acetate and/or tert-butyl methyl ether causing crystallization being used.

With regard to the Office Action objection of the claims being indefinite and requiring all steps of example 1 to be included in the claim, Applicant respectfully traverses this requirement. The Examples are illustrative and are not intended to limit the claimed process. The steps up to the quaternization in claim 13 are known to those in the art. A person skilled in the art knows how to get to the diastereomer mixture which is the starting material for the separation process. The claimed invention is characterized by the choice of the suitable solvents for the recrystallization. Additionally, Applicant asserts that process steps are present in the claim. Applicant respectfully asserts the positive steps of "combining," "recrystallizing," and "precipitating," are process steps that have the requisite particularity and distinctness to those with ordinary skill in the art as required by 35 USC 112. Applicant respectfully requests reconsideration and withdrawal of this

rejection.

II. Rejection under 35 USC 102(b)

Claims 13-32 have been rejected under 35 USC 102(b) as anticipated by Noe, et al. (U.S. Patent 6,307,060, the '060 patent). Applicant respectfully traverses this rejection. Claims 13 is amended herein.

The subject invention is claiming a process. As stated above in regards to the rejection under 35 USC 112, the process has the positive steps of "combining," "recrystallizing," and "precipitating," Thus, there are concrete process steps.

Page 3 of the Office Action states that "Applicants claim a process of making substituted glycopyrronium bromide or iodide but do not claim any process steps" This is not correct.

The process claimed in the present invention is for the separation of diastereomers of glycopyrronium salts. The invention is not for the production of glycopyrronium salts, as described in the Office Action and disclosed in the '060 patent.

Additionally, as stated above, the concrete process steps are present in the claim.

The present invention has arrived at a process that achieves the desired results of precipitating the desired stereoisomer from glycopyrronium salts.

The '060 patent has no disclosure for this process. Applicant reminds the Office:

"[A]nticipation under § 102 can be found only when the reference discloses exactly what is claimed and that where there are differences between the reference disclosure and the claim, the rejection must be based on § 103 which takes differences into account." *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985).

Claim 13 is respectfully asserted not anticipated by the '060 patent because claim 13 requires, precipitating with branched and unbranched alcohols having one to four carbon atoms, acetone, butanone and acetonitrile; and re-crystallization with a second solvent selected from ethyl acetate and/or tert-butyl methyl ether. Thus the '060 is deficient in failing to have the requisite disclosure to anticipate the claim.

Because of the failure of the '060 patent to anticipate the claimed invention, applicant asserts a rejection under 35 USC 102(b) cannot be properly applied.

Applicant respectfully request reconsideration and withdrawal of this rejection.

II. REJECTION UNDER 35 USC 103(a)

The Office Action as sets forth that the currently pending claims may rejected as being obvious over the '060 reference of record.

Applicant respectfully traverses this rejection.

As set forth above, the current invention as now claimed, is a process for

separation of diastereomers of glycopyrronium salts by precipitating with branched and unbranched alcohols having one to four carbon atoms, acetone, butanone and acetonitrile; and re-crystallization with a second solvent selected from ethyl acetate and/or tert-butyl methyl ether. The process steps are neither taught nor suggested in the cited '060 patent. The '060 patent only discloses glycopyrronium salts and does not disclose any of the process steps for the separation of stereoisomers.

The solvents in claim 13 distinguishes the present invention from the '060 patent because the 060 uses chiral tartaric acid for the separation of the racemate. The present invention differs from this process by providing a simplified process for the preparation of enantiomerically pure glycopyrronium compound. This process would not be obvious to the skilled person, as there are numerous solvents to be used in the process, and the selection of the solvents which can be successfully used in separation the diastereomer mixture are not obvious form any prior art disclosure.

The Office Action states (page 4) that the difference between the present invention and the cited prior art is that the '060 patent claims a broader class of compounds than the instant application.

This is not correct as the present application does not claim any compound, but only a process for the separation of the diastereomer mixture.

Further, the current Office Action states that the process disclosed in the present invention and the prior art are essentially the same, and that it is obvious to modify

parameters as concentration, temperature etc. to obtain an optimum result (page 5). This is not the case with the present invention. The present invention does not claim the whole process for the preparation of the glycopyrronium compounds but only the process of diastereomer mixture separation. There is a large difference between the present invention and prior art, as the prior methods for the separation of pure enantiomers from a mixture is the reaction with optically pure reagents. The prior method is applied in the '060 patent using optically pure enantiomers of tartaric acid. This is in contradistinction to the present invention that uses simple non-chiral solvents for the separation, and therefore this step is very different from the one in the '060 patent. Moreover, because there are so many different non-chiral solvents, it is not possible to expect a certain result.

The Office Action summarily dismisses (on page 5) that it is known how to produce compounds in the stereo isomer form. Applicant does not argue stereoisomer isolation is not known. Applicant asserts the process claimed in the subject application is a novel process for the separation of diastereomers of glycopyrronium salts which has neither been taught nor suggested prior to the subject application.

Applicant reminds the Office of the long-standing principle that the chemical arts are highly unpredictable and require a higher standard for obviousness determinations.

Although there is a vast amount of knowledge about general relationships in the chemical arts, chemistry is still largely empirical, and there is often great difficulty in predicting precisely how a given compound will behave. *In re Dillon*, 919 F.2d 688, 710 (Fed. Cir. 1990).

There is no disclosure in the '060 patent, for the process for the separation of diastereomers of glycopyrronium salts as presently claimed.

In view of the failure of the '060 patent to teach, suggest, or provide any type of motivation to modify, in order to arrive at the claimed process for the separation of diastereomers of glycopyrronium salts, Applicant asserts a rejection under 35 USC 103(a) cannot be properly applied. Applicant respectfully requests reconsideration and withdrawal of this rejection.

Based upon the amendments and representations presented herein, Applicant respectfully asserts the application is now in condition for allowance. If the Examiner believes there any issues that have not been resolved the Examiner is invited to call the undersigned representative who is attorney of record in this case.

In view of the foregoing, reconsideration and allowance of claims 13-32 are respectfully solicited.

Please charge any fees which might be due with respect to Sections 1.16 and 1.17
to Deposit Account No. 12-1099 of Lerner Greenberg Stemer LLP.

Respectfully submitted,

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September 23, 2008

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